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Task-residual functional connectivity of language and attention networks

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ABSTRACT

Functional connectivity using task-residual data capitalizes on remaining variance after mean task-related signal is removed from a time series. The degree of network specificity in language and attention domains featured by task-residual and resting-state data types were compared. Functional connectivity based on task-residual data evidenced stronger laterality of the language and attention connections and thus greater network specificity compared to resting-state functional connectivity of the same connections. Covariance between network nodes of task-residuals may thus reflect the degree to which two regions are coordinated in their specific activity, rather than a general shared co-activation. Task-residual functional connectivity provides complementary data to that of resting-state, emphasizing network relationships during task engagement.

1. Introduction

The purpose of this study was to compare the sensitivity of task-residual and resting-state functional connectivity in addressing domain-specific and domain-general connectivity related to language production, using a simple, transparent method.

1.1. Task-residual and resting-state fMRI for determining functional connectivity

Resting-state functional connectivity (rsFC) MRI is the dominant methodology used to capture functional connectivity networks (Biswal et al., 2010; Greicius, Supekar, Menon, & Dougherty, 2009). Task-residual functional connectivity (trFC) is an alternative approach that may offer additional information about coherence of brain systems. In trFC analysis, the effects of an active block or event-related task are regressed out of the fMRI time series and the resulting residual time series is used to define a covariance matrix (Fair et al., 2007; Andrews-Hanna et al., 2007; Fornito, Harrison, Zalesky, & Simons, 2012; Zhang & Li, 2010). Residuals are typically considered error variance when calculating the mean task-evoked signal. However, areas that are functionally related still show covariation and are related to behavioral differences (Al-Aidroos, Said, & Turk-Browne, 2012; Davies-Thompson & Andrews, 2012).

Task-residual functional connectivity may provide more specific information about networks in cognitive states than resting-state functional connectivity (Fair et al., 2007; Rogers & Gore, 2008; Norman-Haignere, McCarthy, Chun, & Turk-Browne, 2011). When the mean effects of the task are regressed out, block-by-block (or trial-by-trial) variability relevant to the task remains in the residual signal (Fair et al., 2007). Block-by-block variability may encompass coordinated activity not consistently represented in modeling techniques of the hemodynamic response function that assume time invariance. As items differ in their neural demands (e.g., variation in task difficulty between individual items or blocks), functional network components that co-operate to meet those demands may show covarying fluctuations. Thus, in analysis techniques assuming time invariance, the activity associated with individual items and/or blocks is not captured in the task signal but may accumulate in the residuals (Fair et al., 2007). Thus, trFC may be more sensitive to functional interactions of specific, task-relevant network connections compared to rsFC.

1.2. Functional connectivity networks related to language

In the present study, participants completed a resting-state scan and a covert verbal fluency task (semantic and phonemic word generation)

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as part of a larger project (Cognitive Connectome Project; Gess, Fausett, Kearney-Ramos, Kilts, James, 2014). To observe activity related to language function during the verbal fluency task, strength of laterality was used (left-hemisphere functional connectivity compared to functional connectivity of right-hemisphere homologues). Because language networks are known to be left-hemisphere lateralized and task-residual data may contain time-invariant effects of the language task, our central hypothesis was that language-based task-residual data would show stronger left-hemisphere lateralization than resting-state data. We used three network relationships to demonstrate our central hypothesis.

The three network relationships used to examine functional connectivity were the following: (1) nodes within the domain-specific language network, (2) nodes that intersect language and attention networks, and (3) nodes within the domain-general intention-attention network. We hypothesized that in each of the three network relationships, task-residual data would show stronger left-lateralized functional connectivity than resting-state data. The first network (language) nodes were comprised of cortex in Broca's area of the inferior frontal gyrus (IFG) and the posterior perisylvian region (PPS) (Binder, Desai, Graves, & Conant, 2009; Zlatar et al., 2013), based on their involvement in verbal fluency tasks. Given the positive correlation between these two regions (Tomasi & Volkow, 2012), we expected functional connectivity between the IFG and PPS to show stronger left-lateralized functional connectivity in task-residual data compared to resting-state data.

The second network relationship investigated was the intersection between anterior language and posterior attention nodes. Portions of PPS, such as the angular gyrus, are involved in both the task-positive language network and task-negative default mode network (DMN) (Wirth et al., 2011; Davey et al., 2015; Humphreys & Lambon Ralph, 2014). Posterolateral DMN regions included the angular gyrus are believed to be involved in self-referential attention and internal processes (Wirth et al., 2011) and show deactivation during effortful language tasks (Seghier, Fagan, & Price, 2010; Meinzer et al., 2012). In resting-state functional connectivity studies, goal-directed regions, such as the IFG, and DMN attention regions typically show an inverse functional relationship, also referred to as an anticorrelation (Fox, Corbetta, Snyder, Vincent, & Raichle, 2006). We thus expected the left IFG (task-positive) and areas of the left PPS converging with DMN functions (task-negative) to be anti-correlated. We expected this anti-correlation to have stronger left-lateralized functional connectivity in task-residual data compared to resting-state data.

The third network relationship of investigation comprised nodes of the domain-general executive attention, or intention-attention network. The pre-supplementary motor area (pre-SMA) was used for its involvement in task-positive activity and intentional response selection relevant to verbal fluency (Lau, Rogers, Haggard, & Passingham, 2004; Nachev, Wydell, O'Neill, Husain, & Kennard, 2007). The posterior cingulate/precuneus (PC/Pc) region is associated with the DMN and involved in various forms of attention, (Cato et al., 2004; Cavanna & Trimble, 2006; Nadeau, Hammond, Williamson, & Crosson, 1997; Vanhaudenhuyse et al., 2010). These two anterior and posterior regions are consistently found to be anti-correlated in resting-state functional connectivity literature, such that as dorsal anterior goal-directed regions (e.g., pre-SMA) are invoked (Fox, Corbetta, et al., 2006), activity in the posterior attentional regions is suppressed (Fox et al., 2005). Thus, we expected an anti-correlation between these two network nodes that would have stronger left-lateralized functional connectivity in task-residual data compared to resting-state data.

2. Method

2.1. Participants

A subset of 21 participants were selected from participants recruited for a parent study, the Cognitive Connectome Project at the University of Arkansas for Medical Sciences (UAMS) (Gess et al., 2014). The parent study consisted of healthy adults between the ages of 18–50. Study procedures were approved by the UAMS Institutional Review Board in accordance with the Declaration of Helsinki. Informed consent was obtained for all participants in the study. Inclusion criteria for this study were healthy right-handed, native English speakers with at least an eighth-grade reading and writing proficiency. We restricted the age range (18–30) of our adult sample because age-related functional alterations are evident at midlife (McGregor, Patten, Kleim, Crosson, & Butler, 2013). Other exclusion criteria and recruitment procedures are described in a previous study (Gess et al., 2014). Demographic information for the sample is presented in Table 1.

Table 1
Demographic characteristics.

Number of participants	21
Age (years)	
Mean (SD)	23.24 (2.57)
Range	18–30
Sex, *n* (%)	
Female	12 (57)
Male	9 (43)
Ethnicity, *n* (%)	
African American	8 (38)
Caucasian	12 (57)
Hispanic Latino	0
Other	1 (5)

2.2. Verbal fluency task and resting-state scans

During the MRI session, participants were asked to silently generate as many words as possible that began with a specific category or letter prompt. Covert word generation has shown to reliably recruit language regions while minimizing motion artifact (La et al., 2016). The task consisted of one run containing 15-s blocks of alternating letter and semantic category prompts separated by 15 s of rest. The letter or cue word was presented for the entire 15 s of word generation. A total of five letters (i.e., R, P, W, S, J) and five categories (i.e., plants & flowers, clothing, foods, states, jobs) were presented. During rest (non-task) blocks, participants were shown a screen-centered fixation cross, and instructed to cease word generation until the next trial. For the resting-state scan, participants were instructed to relax, rest, and keep their eyes focused on the fixation cross in the center of the screen for the 7-min acquisition.

2.3. Scanning procedures

Imaging data were acquired using a Philips 3T Achieva X-series MRI scanner. Anatomic images were acquired with a MPRAGE sequence with the following parameters: matrix = 256 × 256; 22 sagittal slices; TR = shortest; TE = shortest; FA = 8°; resolution = 0.94 × 0.94 × 1 mm^3. Functional images for the early participants (1–50) were acquired using an 8-channel head coil with an echo planar imaging (EPI) sequence and the following parameters: TR = 2000 ms; TE = 30 ms; FA = 90°; FOV = 240 × 240 mm^2; matrix = 80 × 80, 37 oblique slices parallel to orbitofrontal cortex; "Philips interleaved" for participants 1–28 and interleaved for participants 29–49; resolution = 3.0 × 3.0 × 4.0 mm^3. Functional images for the remaining participants (51–79) were acquired using a 32-channel head coil with the following parameters: TR = 2000 ms; TE = 30 ms; FA = 90°; FOV = 240 × 240 mm; matrix = 80 × 80, 37 oblique axial slices parallel to orbitofrontal cortex; sequential ascending acquisition; slice thickness = 2.5 mm with a 0.5 mm gap, resolution = 3.0 × 3.0 × 3.0 mm^3. Three image volumes (6s) at the beginning of each functional run were discarded to allow the spin lattice magnetization to stabilize.